

REMARKS

A. Status of the Claims

Claims 9-10 and 14-22 were pending at the time of the Action. Claim 9 has been amended to delete the phrase “or preventing” and to include language that refers back to the method recited in the preamble.

B. The Claims Are Enabled

The Action rejects claims 9-10 and 14-22 as failing to comply with the enablement requirement under 35 U.S.C. § 112, first paragraph. The Action acknowledges that the specification is enabling for treating neurodermatitis or psoriasis, but alleges that the specification is not enabling for preventing neurodermatitis or psoriasis. The Action states that “prevention” requires that the skin disease be prevented in every case and that the skin disease never re-occurs (Action, p. 4). While Applicant generally disagrees with this characterization of the term “prevention,” Applicant has deleted this term from claim 9. The alleged basis for this rejection is obviated by this amendment. Applicant, therefore, requests that this rejection be withdrawn.

C. The Claims Are Patentable Over Fuchs in View of SU 1740002 or Buhlbacker

The Action rejects claims 9-10 and 14-22 under 35 U.S.C. § 103(a) as obvious over Fuchs *et al.* (WO 01/97634 A1) in view of SU 1740002 (as explained in the Russian Search Report) or Buhlbacker. Applicant traverses this rejection.

The currently claimed method of treating neurodermatitis or psoriasis is non-obvious over the cited references because the results of the claimed method were unexpected. As described in the present specification, Buhlbacker disclosed the use of native mare’s milk as a food additive in the treatment of neurodermatitis. Buhlbacker, however, found that the dietetic treatment required

a minimum treatment time of ***10 months***. In addition, Buhlbacker reported that mare's milk was ***ineffective*** in treating neurodermatitis if given alone.

SU 1740002 describes the use of koumiss as a dietary supplement in the treatment of neurodermatitis and eczema. Applicant has enclosed a translation of SU 1740002 for the Examiner's convenience. Koumiss is a fermented beverage that is traditionally made from mare's milk. The fermentation process results in a number of changes to the milk. For example, the lactose is converted to alcohol. As noted in SU 1740002, the sedative effect of koumiss, which is likely due to the alcohol content, results in more sound sleep, reduction in skin itching, and relief of high nerve excitability (SU 1740002 at page 4). However, since mare's milk does not contain alcohol, one could not have predicted a similar beneficial effect of mare's milk based on the above-mentioned properties of koumiss, much less the utility of the current invention for treating neurodermatitis and psoriasis.

As a further example, SU 1740002 discloses that koumiss has antibacterial properties (SU 1740002 at page 4). These antibiotic properties are likely attributable to the active cultures involved in the fermentation process. Mare's milk, however, is not fermented by such cultures, thus one could not have predicted a similar antibiotic property of mare's milk based on the above-mentioned property of koumiss.

Fuchs discloses that highly unsaturated fatty acids are important for skin metabolism (Fuchs translation, p. 3). Highly unsaturated fatty acids occur mainly in plant oils and fish oil (Fuchs translation, p. 3). While Fuchs also discloses that milk may be added to the matrix and fatty acid mixture before drying (Fuchs translation, p. 15), there is no specific disclosure or suggestion that a milk concentrate dried on a biologically inert, disperse matrix can be used in a method treating neurodermatitis or psoriasis.

In summary, a review of the content of the cited art reveals that none of the references specifically disclose that a mare's milk concentrate dried on a biologically inert, disperse matrix can be used in a method of treating neurodermatitis or psoriasis. SU 1740002 reported the use of koumiss as a dietary supplement in the treatment of neurodermatitis and eczema, and Fuchs reported that highly unsaturated fatty acids, such as those that occur in plant and fish oils, are important for skin metabolism. Buhlbacker disclosed the use of native mare's milk, but not a dried mare's milk concentrate, as a food additive in the treatment of neurodermatitis. Buhlbacker, however, found that the dietetic treatment required a minimum treatment time of **10 months** and that mare's milk was *ineffective* in treating neurodermatitis if given alone. Thus, not only does the cited art fail to disclose that a mare's milk concentrate dried on a biologically inert, disperse matrix can be used in a method of treating neurodermatitis or psoriasis, but the cited art also fails to provide a reasonable expectation of success in doing so.

In the working examples provided in the present specification marked improvement in symptoms were reported in the three neurodermatitis patients given the dried mare's milk preparation (Examples 1-3, p. 24-28). This improvement was evident at the first follow-up visit at **one month** and was sustained over the course of the study. In addition, the only other measures taken by the patients were greasing ointments and oil baths. These results would not have been predicted from Buhlbacker's disclosure that the dietetic treatment with native mare's milk required a minimum treatment time of **10 months**. These results also could not have been predicted from Fuchs or SU 1740002, which provided no data regarding treatments with either native mare's milk or a dried mare's milk concentrate.

Additionally, Examples 4-6 (pages 30-34) in the specification demonstrated a clear and sustained improvement in three reported psoriasis patients given the dried mare's milk preparation. The improvement was evidence in all three patients at the first follow-up visit at six

weeks. As with the neurodermatitis cases discussed in the preceding paragraph, these results could not have been predicted from Buhlbacker, Fuchs, and SU 1740002.

“A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 127 S.Ct. at 1741. Furthermore, the Supreme Court noted that when the combined elements work together in an unexpected and fruitful manner, this is evidence that the combination was not obvious. *Id.* at 1741. As discussed above, an orally administered composition comprising a mare milk concentrate dried on a biologically inert, disperse matrix, provided a marked and sustained improvement in patients with neurodermatitis and psoriasis that could not have been predicted from the cited references. For at least these reasons, the current claims are non-obvious over Buhlbacker, Fuchs, and SU 1740002. Applicant, therefore, requests the withdrawal of this rejection.

D. Conclusion

Applicant believes this to be a complete reply to the Office Action dated July 26, 2007, and respectfully requests favorable consideration of the claims in view of the amendments and statements contained herein.

The Examiner is invited to contact the undersigned attorney with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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(56) Akhmetova M.A. et al.. The problems of nutrition of a healthy and sick child. Alma-Aty, 1980, p.76

(54) METHOD OF TREATMENT OF ALLERGODERMATOSES IN CHILDREN

(57) The invention relates to medicine, specifically pediatrics, allergology and dietary cure. Object – to reduce the time of treatment and elongation of remission of a disease, for which purpose koumiss is administered in the presence of hypoallergen diet, 25 ml/kg of a body weight, twice a day, one tablet.

The invention relates to medicine, particularly pediatrics, allergology, and dietary cure.

An object of invention – reduction of the time of treatment and lengthening of remission of a disease.

Said object is achieved owing to the fact that according to a method of the dietary cure of allergodermatoses, in the presence of a hypoallergen diet, koumiss is administered to children twice a day as a lunch and in the afternoon, 25.0 ml per kg of a body weight daily. A

ration is devoid of other milk products. Conventional symptomatic and local treatment of diseases is carried out along with said dietary cure.

Example 1. Patient G., aged 10; diagnosis: neurodermit. Limited form. Average severity course. Coli-disbacteriosis, II Degree.

Since the age of two months, the child has shown symptoms of exudative – catarrhal diathesis associated with a change-over to artificial bringing-up. Child's eczema developed afterwards that transformed into neurodermit. A specific feature of family history is allergization: in the grandmother, mother's line—obesity, bronchial asthma; pollinosis – in the mother. Reactions of enhanced sensitivity were observed in the child to some food products (citrus fruit, chocolate, carrots, tomatoes). Observed by an allergist, underwent treatment in hospital many a time. On examination, inflammatory changes observed in the area of bends of the upper and lower limbs on the skin in the form of incrustated plaques on an infiltrated base. Itching. Hemogram: zozinophilia about 10%. According to PRIST data the total IgE level is 600 Ki/ml; sensitization to a chick egg white revealed. Using a method of degranulation of fatty cells sensitization observed to cow milk chick egg albumins. A course of dietary cure carried out by the method proposed. The result: a rapid, marked improvement of general conditions. Regression of skin inflammatory symptoms since the fifth day of treatment, their complete disappearance on the 25th day of the start of treatment. Hemogram: a reduced amount of zozinophils. Dung assay: the improved picture of a microbiocenosis of the intestines. Positive dynamics according to PRIST and RAST data and fatty cells degranulation. The child gained 400.0 g in weight over a period of treatment. Released with complete remission.

Example 2. Patient A. Aged 6 years. Diagnosis: neurodermit. Common form. Critically ill. Period of exacerbation. Disbacteriosis, fungous, II Degree. Suffers from child's eczeme since the age of two years that transformed into neurodermit. Family history burdened by allergologic diseases: mother's line—medicamental allergy in the uncle.

On inspection, a cutaneous process is of a common nature, alterations on the skin and in the form of grouped papule plaques localized in the area of the neck, the chest, bends of the upper and lower limbs against an infiltrated background. Zones of lichenification, desquamation, cracks, combing. Hemogram: zozinophilia about 8%. On examination of excrements for disbacteriosis, fungous coli-bacteriosis, II Degree, detected due to the presence of fungi of the genus Misoch, absence of lactobacilli in a 10^{-3} titer. According to PRIST, the total IgE is 1000 Ki/ml. According to RAST, sensitization was revealed to a cow milk albumin, according to degranulation of fat cells – to cow milk/chicken egg albumins. A course of dietary cure was carried out according to the claimed method. The result: rapid regression of skin alterations in killing zones with the complete remedy of inflammatory symptoms, improvement of general conditions. Hemogram: a reduced amount of zozinophils. Examination of excrements: the reduced intensity of a disbacteriosis of the intestines transformed from II Degree into I Degree because of the appearance of lactobacilli in a 10^{-1} titer, disappearance of fungi of the genus Misoch. As a result of a course of dietary cure under the method proposed a clear-cut dynamics of indices was observed to characterize the level of sensitization according to the method of degranulation of fatty cells and the PRIST. The child released on the 26th day in a state of complete clinic convalescence.

The method was tested in the Kazakh Research Institute of Pediatrics on 40 children having allergodermatoses.

The method is carried out in the following fashion.

The dietetic product used is represented by koumiss administered twice a day during a lunch and in the afternoon, 25.0 ml per kg of a body weight daily. Dietary cure is carried out in the presence of a hypoallergen diet, with milk products eliminated from the ration. The entire course of treatment 20-25 days. Said dietary cure is carried out concurrently with common symptomatic and local treatment. The result: improvement of general conditions and state of health, regression of skin inflammatory symptoms on the 5th – 7th day of

hospitalization, their complete disappearance on the 24th day. Hemogram: a reduced amount of zozinophils. Dung assay: an improved picture of microbiocenosis of the intestines, an increased body weight. Patients stay in hospital on the average 24 days. Positive dynamics is likewise observed according to PRIST and RAST data, degranulation of fatty cells, which fact affirms sensitization.

Realization of dietary cure effects is observed in periods markedly earlier than said dietary cure using a lactic acid product "Baldyrgan". Remission extends. (Cf. Table).

In the format of the method as proposed, koumiss produces comprehensive effects on a patient's organism:

elimination of cause-significant antigens because sensitization to cow milk albumins occurs most frequently;

normalizing effects on a microbiocenosis of the intestines due to the antibiotic properties, because in the overwhelming majority of patients there is observed a disbacteriosis of the intestines and the synthesis of vitamins is disturbed by the intestinal microflora;

owing to the fact that koumiss has a full value amino acid formulation and said koumiss albumins are represented by generally a readily available albumin fraction said koumiss makes good an albumin loss quite well that occurs in connection with a cutaneous and inflammatory process (festering, desquamation);

on account of the sedative effect of koumiss, patients' sleep becomes more sound, skin intense itching abates, and high nerve excitability is relieved.

Thus, the method of dietary cure as proposed is more effective than the conventional, which fact is attributable to pathogenetic adequacy of a diet for children who suffer from the cutaneous forms of allergic diseases.

CLAIMS

A method of dietary cure of allergodermatoses in children comprising administering lactic acid products, characterized in that the reduce the time of treatment and lengthen the remission of a disease, use is made of koumiss on the basis of 25 ml/kg of a body weight twice a day.

Dynamics of clinical manifestations
in patients suffering from allergodermatoses
in the presence of various diets

Group	Number	Improvement of general condition and state of health, days, from start of treatment	Regression of inflammatory process on skin, days from start of treatment	Time of treatment, days	Duration of remission, months
“Baldyrgan” diet (known method)	98	11±0.3	32.1±2.17	40±1.0	20±2.1
Koumiss diet (proposed method)	40	6±0.19 $p \leq 0.01$	26±1.31 $p \leq 0.01$	27±1.9 $p \leq 0.01$	28±2.3 $p \leq 0.01$

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